

REMARKS

Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

I. Status of Claims

1. Claims 1-34 and 39-76 are currently pending in the present application.
2. Claims 69 has been amended to specify the addition of a mercapto compound. Claims 70-74 have been rewritten to be dependent on claim 69. Claims 75 and 76 have been amended to clarify these claims. Support for all these claim amendments is found in the specification, for example, at page 6, lines 4-9 and in Examples 1-7. Applicants request the rejoinder of claims 69-76.
3. Applicants reserve the right to pursue the subject matter of any withdrawn or cancelled claims in one or more continuing applications. The withdrawal and cancellation of claims was done without waiver or prejudice.
4. Following the above amendments claims 1-34 and 39-76 remain pending in the present application.

II. Claim Rejections Under 35 U.S.C. § 103(a)

5. Claims 1-34 and 39-76 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Cunningham et al., US Patent No. 5,849,535, in view of Jespersen et al., and further in view of Houk et al. Applicants respectfully traverse this rejection.
6. The pending claims of the present invention are directed to process for decreasing the amount of an impurity produced in a recombinant production process for growth hormone.
7. The motivation, or suggestion in prior art is what the combination of prior art statements would have suggested to those of ordinary skill, such statements must be considered in context of teaching of entire reference(s), and cannot be viewed in abstract, and rejection of claims cannot be predicated on mere identification in prior art reference of individual components of claimed limitations; rather, particular

findings must be made as to reason skilled artisan, with no knowledge of claimed invention, would have selected these components for combination in manner claimed.

8. The Examiner has focused the outstanding obviousness rejection on the teaching of Jespersen et al., and in particular “the quoted passage” on page 5 of the Final Office Action (emphasis added). While the quoted paragraph notes procedures for renaturation of the trisulphide derivative of BhGH, such procedures were only utilized to confirm the presence of the derivative. Note the statement in the Abstract by the authors that they were not able to find a previous report in the literature about this kind of derivative.

A review of the entire Jespersen et al. reference reveals, however; that the fermentation and processing of the BhGH was essentially carried out by the method of Dalbøge et al. *Biotechnology* (1987), 5, 161-164 (Reference 14) and Jensen, B. and Carlsen, S., *Biotechnology and Bioengineering*, 36, 1-11 (Reference 16), see page 365, column 2, third paragraph. The reference to the Dalbøge et al. paper is also noted in “the quoted paragraph” (emphasis added).

Nowhere does Jespersen et al. advocate a change in the cited protocol of Dalbøge, et al. or of Jensen, E.B. and Carlsen, S. to include a mercapto compound to decrease the trisulfide isoform impurity in a recombinant production and isolation process; nor is this change suggested or provided by the combination of the other cited references.

9. The Examiner also notes at the top of page 5 of the Final Office Action that Jespersen et al. teaches the addition of 1,4-dithiothretol “in-situ” prior to sample preparation and analysis by mass spectroscopy, referring to page 367, column 1, paragraph 2 (emphasis added). The Examiner then argues that Jespersen et al. was successful in finding a solution to reduce the impurity “in-situ” (emphasis added). Applicants disagree with the basis for the rejection, as the mass spectroscopy analysis of Jespersen et al. was only utilized to confirm “sulfur atom content,” see page 369, column 2, Table 1 and the paragraph bridging pages 369 and 370 and these results were stated to be “not conclusive” (emphasis added twice).

Nowhere does Jespersen et al. when taken in combination with Houk et al. and Cunningham teach or suggest to one of skill in the art that the protocol for manufacturing recombinant growth hormone should include the addition of a

mercapto compound as presently claimed. Cunningham post dates the teachings of Jespersen et al. and Houk et al., and it may be argued that one of skill in the art even in possession of Jespersen et al. and Houk et al. would not have been motivated to alter the fermentation and isolation of human growth hormone relying on the “in-situ” data of Jespersen et al. at page 365, column 2, third paragraph (emphasis added).

10. Further, it is respectfully submitted that a proper prima facie obviousness rejection has not been established by the combination of the teachings of Cunningham et al. in view of and Jespersen et al. and further in view of Houk et al.

In determining the propriety of the Patent Office case for prima facie obviousness, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the proposed substitution or other modification.

The Examiner has noted that Cunningham et al. does not use a mercapto compound as reducing agents to decrease the trisulfide impurity. The additional “in-situ” teachings of Jespersen et al and Houg et al. taken in combination with Cunningham et al. fail to provide the additional teachings and motivation to make obvious the use of a mercapto compound to decrease the amount of trisulfide isoform impurity in the claimed recombinant production process for a growth hormone.

11. In view of the above remarks, Applicants request the withdrawal of the obviousness rejection and reconsideration of claims 1-34 and 39-68.

III. REQUEST FOR REJOINDER OF CLAIMS 69-76

12. Applicants request the rejoinder of claims 69-76 in view of the amendments to these claims.

IV. Request for Interview

13. Applicants request a telephonic interview with the Examiner to discuss the merits of the outstanding obviousness rejection.

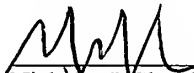
V. Conclusion

14. Applicants submit that all the grounds for rejection of the pending claims have now been overcome and that all the claims are now in condition for allowance, which action is respectfully requested.

15. Applicants have requested a telephonic interview with the Examiner and the Examiner's supervisor to discuss the outstanding obviousness rejection and to help advance prosecution of the application.

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Respectfully submitted,



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